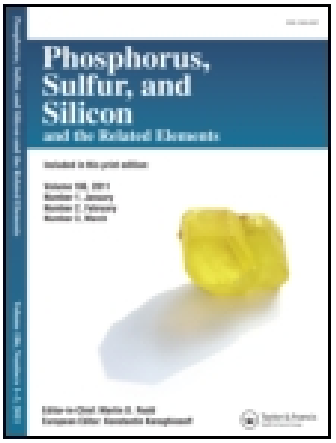

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Reactions with Hydrazonoyl Halides 63: Synthesis and Anticancer Activity of Some New 1,3,4-Thiadiazoles, 1,3,4-Selenadiazoles, and 1,2,4-Triazolo[4,3-a]pyrimidines

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REACTIONS WITH HYDRAZONOYL HALIDES 63: SYNTHESIS AND ANTICANCER ACTIVITY OF SOME NEW 1,3,4-THIADIAZOLES, 1,3,4-SELENADIAZOLES, AND 1,2,4-TRIAZOLO[4,3-*a*]PYRIMIDINES

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2,3-Dihydro-1,3,4-thiadiazoles, 2,3-dihydro-1,3,4-selenadiazoles, and triazolino[4,3-a]pyrimidines containing benzoxazole or benzothiazole moieties were prepared from the reaction of each of ethyl 3-aza-3-(benzoxazol-2-ylamino)-2-chloroprop-2-enoate and ethyl 3-aza-3-(benzothiazolo-2-ylamino)-2-chloroprop-2-enoate with each of potassium thiocyanate, potassium selenocyanate, alkyl carbodithioate, and pyrmidine-2-thione derivatives. All the newly synthesized compounds were confirmed by elemental analysis, spectral data, and alternative route synthesis whenever possible. Some of the newly synthesized compounds were screened toward certain cancer tumors.

Supplemental materials are available for this article. Go to the publisher's online edition of* Phosphorus, Sulfur, and Silicon and the Related Elements *to view the free supplemental file.

Keywords Anticancer activity; hydrazonoyl bromide; 1,3,4-selenadiaziles; 1,3,4-thiadiazoles; triazolo[4,3-a]pyrimidines

INTRODUCTION

Hydrazonoyl halides have been widely employed for the synthesis of heterocyclic compounds.[1–4] 1,3,4-Thiadiazole derivatives have become useful in medicine, agriculture, and in many fields of technology.[5] In addition, 2-(4-aminophenyl)benzothiazole and oxazole and their analogues are a novel class of potent and selective antitumor agents.[6–10] As an extension of our study[11–16] and of our synthesis of 1,3,4-thiadiazoles, we report here the synthesis of hydrazonoyl halides containing 4-phenylbenzothiazole and 4-phenylbenzoxazole moieties and their reactions toward some potassium thiocyanate, potassium selenocyanate, alkyl carbodithioate, and pyrimidine-2-thione derivatives.

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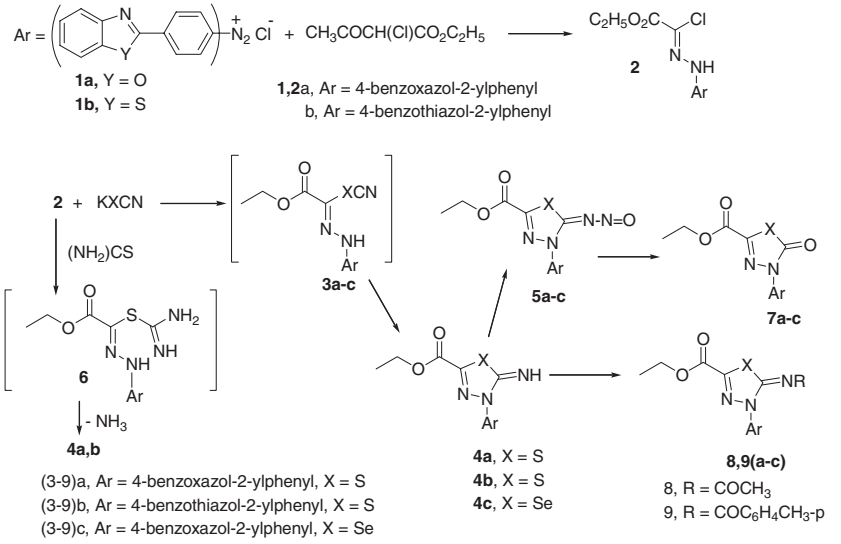
RESULTS AND DISCUSSION

Treatment of the appropriate diazotized [4-(1,3-benzoxazol-2-yl)phenyl]amine[6] (**1a**) and diazotized [4-(1,3-benzothiazol-2-yl)phenyl]amine[10] (**1b**) with ethyl 2-chloro-3-oxobutanoate in ethanolic sodium acetate gave ethyl 3-aza-3-[(benzoxazol-2-ylphenyl)amino]-2-chloroprop-2-enoate (**2a**) and ethyl 3-aza-3-(benzothiazolo-2-ylphenyl)amino]-2-chloroprop-2-enoate (**2b**), respectively. Structure **2** was elucidated by elemental analysis and spectral data. The ^{1}H NMR spectrum of **2a** showed signals at δ = 1.37 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.40 (d, 2H, J = 8Hz, ArH's), 7.50 (d, 2H, J = 8Hz, ArH's), 8.00 (d, 2H, J = 8Hz, ArH's), 8.07 (d, 2H, J = 8Hz, ArH's), and 10.89 (s, br., 1H, NH). Treatment of the appropriate **2a** with each of potassium thiocyanate and potassium selenocyanate gave ethyl 3-(4-(benzoxazol-2-ylphenyl)-2-imino-1,3,4-thiadiazoline-5-carboxylate (**4a**) and ethyl 3-(4-(benzoxazol-2-ylphenyl)-2-imino-1,3,4-selenadiazoline-5-carboxylate (**4c**), respectively (Scheme 1). The structure of **4** was elucidated on the basis of elemental analyses, spectral data, alternative synthetic route, and its nitrosation and acylation reactions.



Scheme 1

In addition, treatment of the appropriate **2a** with thiourea in boiling ethanol gave a product identical in all respects (mp, mixed mp, and spectra) with **4a**. These results indicate that hydrazone **3a** and amidiazone **6a** are not the final products, and that **3a** and **6a** readily gave **4a** either by cyclization or by elimination of one molecule of ammonia (Scheme 1). Acylation of **4a** with acetic anhydride or with 4-methylbenzoyl chloride in pyridine afforded ethyl 2-(1-aza-2-oxopropylidene)-3-(4-benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (**8a**) and ethyl 2-[1-aza-2-(4-methylphenyl)-2-oxoethylidene]-3-(4-benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (**9a**), respectively. Spectral data and elemental analyses confirmed their structures. ^{1}H NMR spectrum of **8a** showed

signals at $\delta = 1.45$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 2.41 (s, 3H, $CH_3CON{=}$), 4.47(q, 2H, $J = 7.5$ Hz, $\mathbf{CH_2}CH_3$), 7.40 (d, 2H, $J = 8$Hz, ArH's), 7.50 (d, 2H, $J = 8$Hz, ArH's), and 8.44 (d, 2H, $J = 8$Hz, ArH's).

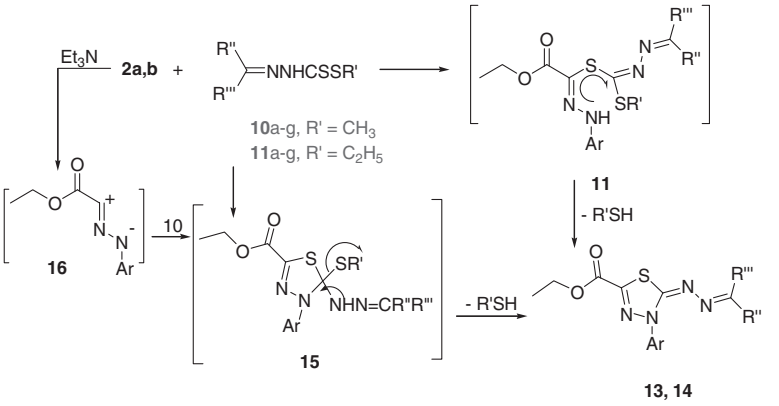
Analogously, acylation of each of **4b** and **4c** gave **8b,c** and **9b,c**, respectively. Nitrosation of each **4a** and **4c** with saturated sodium nitrite in acetic acid at 0–5°C gave ethyl 2-(azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (**5a**) and ethyl 2-(azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-selenadiazoline-5-arboxylate (**5c**), respectively. Ethyl 3-(4-benzoxazol-2-ylphenyl)-2-oxo-1,3,4-thia/selenadiazoline-5-carboxylate **7a,c** and 3-(4-benzothiazol-2-ylphenyl)-2-oxo-1,3,4-thiadiazoline-5-carboxylate **7b** were prepared by thermolysis of **5a,c** and **5b** in boiling xylene. The IR spectrum of **7** revealed a band near $\nu = 1685$ cm^{-1} (CO).

Compound **2a** reacted with the methyl carbodithioates[18,19] **10a** to give the 1,3,4-thiadiazoline derivative **13a**. The structure of **13a** was confirmed by elemental analysis, spectral data, and alternative synthetic route. ^{1}H NMR of **13a** showed signals at $\delta =$ 1.36(t, 3H, $\mathbf{CH_3}CH_2$), 4.39 (q, 2H, $\mathbf{CH_2}CH_3$), 7.54–8.33 (m, 13H, ArH's), and 8.57 CH (vinyl)). Also, treatment of **2a** with ethyl carbodithioates **11a** in ethanolic triethylamine gave a product identical in all respects (mp, mixed mp, and spectra) with **13a**. Product **13a** was assumed to be formed via elimination of alkanethiol (R^1SH) from the corresponding cycloadduct **15**, which formed from 1,3-dipolar cycloaddition (or 1,3-addition) of nitrile imide **16** (generated in situ from hydrazonoyl chlorides **2** and triethylamine) to C=S **14** (Scheme 2). Analogously, treatment of the appropriate **2a,b** with the appropriate **10a–g** (or **11a–g**) in ethanolic triethylamie gave the thiadiazolines **13a–g** and **14 a–g**, respectively (Scheme 2).

Next, treatment of ethyl 4-methyl-6-phenyl-2-thioxo-1,3,6-trihydro-pyrimidine-5-carboxylate (**17a**) with **2a** in chloroform and triethylamine gave the 1,2,4-triazolo[4,3-*a*]pyrimidine-5-carboxylates **20a**. The structure of **20a** was elucidated by elemental analysis, spectra, and alternative synthesis. The ^{1}H NMR spectrum of **20a** showed signals at $\delta =$ 1.23 (t, 3H, $\mathbf{CH_3}CH_2$), 1.12 (t, 3H, $\mathbf{CH_3}CH_2$), 2.88 (s, 3H, CH_3), 4.02 (q, 2H, $\mathbf{CH_2}CH_3$), 4.11 (q, 2H, $\mathbf{CH_2}CH_3$), 6.67 (s, 1H, CH), and 6.8–8.43 (m, 13H, ArH). Its IR spectrum revealed bands at $\nu = 1735$ cm^{-1} (CO). Ethyl 6-methyl-4-[4-phenyl-2-methylthio-3,4-dihydropyrimidine-5-carboxylate (**22a**) reacted with **2a** in boiling ethanolic sodium ethoxide solution gave products identical in all aspects (mp, mixed mp, and spectra) with the corresponding **20a**. Analogously, treatment of each **2a** with the appropriate **17b,c** and **2b** with the appropriate **17a–c** gave triazolo[4,3-*a*]pyrimidines **20b,c** and **21a–c**, respectively (Scheme 3).

The formation of **20** can be explained via 1,3-dipolar cycloaddition or 1,3-addition of nitrile imide **16** (prepared in situ from hydrazonoyl chlorides **2** with triethylamine or sodium ethoxide) to C=S of **16** (or NH of **22**) to give intermediate **18** (or **23**), with ring opening and ring closure to afford the final products **20** by elimination of hydrogen sulfide from **19** (or methyl mercaptan from **23**) (Scheme 3).

Treatment of **2a** with methyl benzoylhydrazinecarbodithioate (**24**) in ethanolic triethylamine gave 2,3-dihydro-1,3,4-thiadiazole **26** (Scheme 4). Its structure was elucidated by elemental analysis, spectral data, and alternative synthetic route. The ^{1}H NMR spectrum showed signals at $\delta = 1.39$ (t, 3H, $\mathbf{CH_3}CH_2$), 4.42 (q, 2H, $CH_3\mathbf{CH_2}$), 7.42–8.35 (m, 13H, ArH), and 11.42 (s, br, 1H, NH). Thus, treatment of **2a** with 5-phenyl-1,3,4-oxadiazole-2-thiol (**27**) gave products identical in all respects (mp, mixed mp, and spectra) with **26a** (Scheme 4). Similarly, treatment of the appropriate **2a,b** with **28** gave thiadiazolines **29a** and **29b**, respectively.



10a, R'' = H, R''' = C_6H_5 , R' = CH_3
b, R'' = H, R''' = 2,3-$(OCH_2O)C_6H_3$, R' = CH_3
c, R'' = H, R''' = 4-$(CH_3)_2CHC_6H_4$, R' = CH_3
d, R'' = CH_3, R''' = C_6H_5, R' = CH_3,
e, R'' = CH_3, R''' = 2-C_4H_3O, R' = CH_3
f, R''-R''' = 1,2-C_6H_4(NHCOC=), R' = CH_3
g, R''-R''' =1,2-C_6H_4(COC=CO), R' = CH_3

11a, R'' = H, R''' = C_6H_5, R' = C_2H_5
b, R'' = H, R''' = 2,3-$(OCH_2O)C_6H_3$, R' = C_2H_5
c, R'' = H, R''' = 4-$(CH_3)_2CHC_6H_4$, R' = C_2H_5
d, R'' = CH_3, R''' = C_6H_5, R' = C_2H_5
e, R'' = CH_3, R''' = 2-C_4H_3O, R' = C_2H_5
f, R''-R''' = 1,2-C_6H_4(NHCOC=), R' = C_2H_5
g, R''-R''' =1,2-C_6H_4(COC=CO), R' = C_2H_5

13a, R'' = H, R''' = C_6H_5, Ar = 4-benzoxazol-2-ylphenyl
b, R'' = H, R''' = 2,3-$(OCH_2O)C_6H_3$, Ar = 4-benzoxazol-2-ylphenyl
c, R'' = H, R''' = 4-$(CH_3)_2CHC_6H_4$, Ar = 4-benzoxazol-2-ylphenyl
d, R'' = CH_3, R''' = C_6H_5, Ar, Ar = 4-benzoxazol-2-ylphenyl
e, R'' = CH_3, R''' = 2-C_4H_3O, Ar = 4-benzoxazol-2-ylphenyl
f, R''-R''' = 1,2-C_6H_4(NHCOC=), Ar = 4-benzoxazol-2-ylphenyl
g, R''-R''' = 1,2-C_6H_4(COC=CO), Ar = 4-benzoxazol-2-ylphenyl

14a, R'' = H, R''' = C_6H_5, Ar = 4-benzothiazol-2-ylphenyl
b, R'' = H, R''' = 2,3-$(OCH_2O)C_6H_3$, Ar = 4-benzothiazol-2-ylphenyl
c, R'' = H, R''' = 4-$(CH_3)_2CHC_6H_4$, Ar, Ar = 4-benzothiazol-2-ylphenyl
d, R'' = CH_3, R''' = C_6H_5, Ar, Ar = 4-benzothiazol-2-ylphenyl
e, R'' = CH_3, R''' = 2-C_4H_3O, Ar = 4-benzothiazol-2-ylphenyl
f, R''-R''' = 1,2-C_6H_4(NHCOC=), Ar = 4-benzothiazol-2-ylphenyl
g, R''-R''' =1,2-C_6H_4(COC=CO), Ar = 4-benzothiazol-2-ylphenyl

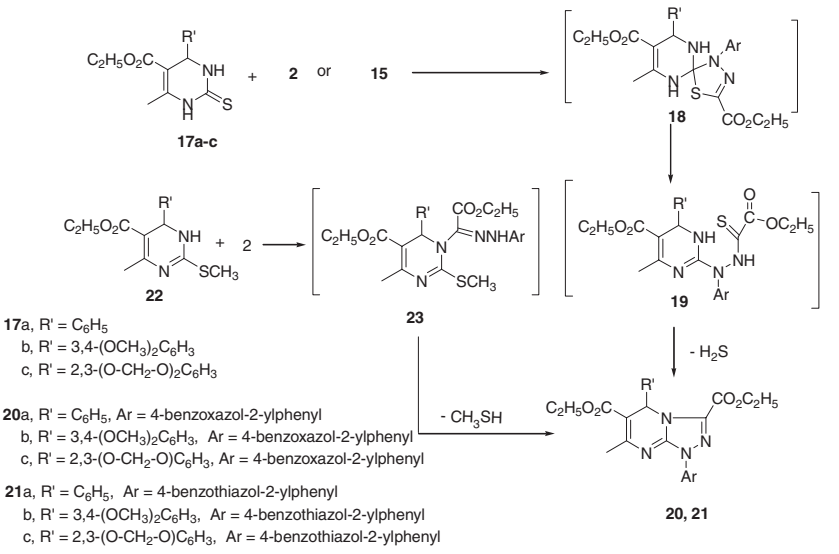
Scheme 2

ANTICANCER AND CYTOTOXIC ACTIVITY

Twelve of the synthesized compounds were subjected to anticancer screening, and some of these compounds showed a cytotoxic effect. Female Swiss albino mice from the Animal House of the Egyptian Cancer Institute were maintained on standard pellet diet and water, and in vitro test for cytotoxic effect was operated using Ehrlich ascites carcinoma (EAC)[17] induced through interperitonial transplantation in female Swiss albino mice. (See the Supplemental Materials, available online, for full details.)

EXPERIMENTAL

All melting points were determined on an electrothermal apparatus and are uncorrected. IR spectra were recorded (KBr discs) on a Shimadzu FT-IR 8201 PC spectrophotometer. ^{1}H NMR spectra were recorded in $CDCl_3$ and $(CD_3)_2SO$ solutions on a Varian

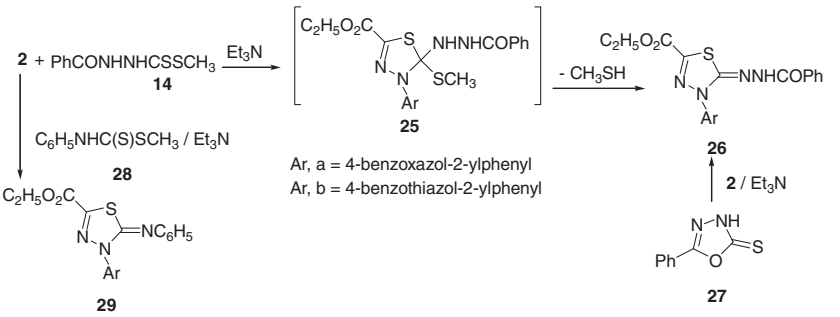


Scheme 3

Gemini 300 MHz spectrometer, and chemical shifts were expressed in δ units using TMS as internal reference. Elemental analyses were carried out at the Microanalytical Center of the Cairo University. Alkyl carbodithioates[18,19] were prepared as previously reported.

Synthesis of Ethyl 3-Aza-3-(benzoxazol-2-ylamino)-2-chloroprop-2-enoate (2a) and Ethyl 3-Aza-3-(benzothiazolo-2-ylamino)-2-chloroprop-2-enoate (2b)

The appropriate amount of diazotized [4-(1,3-benzoxazol-2-yl)phenyl]amine (**1a**) and diazotized [4-(1,3-benzothiazol-2-yl)phenyl]amine (**1b**) (0.005 mol) were added dropwise to cold solution (0°C) of ethyl 2-chlorobutanoate (1.65 g, 0.005 mol) and sodium acetate trihydrate (0.65 g, 0.005 mol) while stirring. The yellow precipitate was collected and recrystallized from ethanol to give **2a** and **2b**, respectively (Tables I and II).



Scheme 4

Table I Characterization data of the newly synthesized compounds

% Analyses, Calcd./Found				Mol. Formula	Yield[a]%	Mp, °C	Compound
S	N	H	C	Mol. Wt.	Color	Solvent	no.
—	12.22	4.10	59.40	$C_{17}H_{14}ClN_3O_3$	82	199–201	**2a**
	12.02	3.99	59.23	343.76	Yellow	EtOH	
8.91	11.68	3.92	56.74	$C_{17}H_{14}ClN_3O_2S$	80	172–174	**2b**
9.01	11.79	3.99	56.59	359.83	Orange	EtOH	
8.75	15.29	3.85	59.01	$C_{18}H_{14}N_4O_3S$	60	170–174	**4a**
8.59	15.32	3.77	59.12	366.39	Brown	EtOH	
16.77	14.65	3.69	56.53	$C_{18}H_{14}N_4O_2S_2$	60	165–168	**4b**
16.70	14.65	3.80	56.66	382.46	Brown	EtOH	
—	13.56	3.41	52.31	$C_{18}H_{14}N_4O_3Se$	65	169–170	**4c**
	13.50	3.32	52.32	413.29	Brown	EtOH	
8.11	17.71	3.31	54.68	$C_{18}H_{13}N_5O_4S$	85	134–137	**5a**
8.01	17.65	3.22	54.60	395.39	Red	Acetone	
15.59	17.02	3.18	52.54	$C_{18}H_{13}N_5O_3S_2$	80	128–131	**5b**
15.48	16.99	3.10	52.44	411.46	Pale rose	Acetone	
—	15.83	2.96	48.88	$C_{18}H_{13}N_5O_4Se$	80	134–137	**5c**
	15.75	3.01	48.75	442.29	Pale rose	Acetone	
8.73	11.44	3.57	58.85	$C_{18}H_{13}N_3O_4S$	60	155–157	**7a**
8.70	11.41	3.77	58.77	367.38	Shiny yellow	EtOH	
16.72	10.96	3.42	56.38	$C_{18}H_{13}N_3O_3S_2$	65	151–155	**7b**
16.66	11.01	3.32	56.30	383.44	Shiny yellow	EtOH	
—	10.14	3.16	52.19	$C_{18}H_{13}N_3O_4Se$	60	124–125	**7c**
	9.86	3.11	52.09	414.27	Shiny yellow	DMF/EtOH	
7.85	13.72	3.95	58.81	$C_{20}H_{16}N_4O_4S$	85	164–166	**8a**
7.69	13.69	3.79	58.79	408.43	Buff	EtOH	
15.11	13.20	3.80	56.59	$C_{20}H_{16}N_4O_3S_2$	80	155–156	**8b**
1501	13.30	3.87	56.55	424.5	Buff	DMF/EtOH	
—	12.30	3.54	52.76	$C_{20}H_{16}N_4O_4Se$	80	152–154	**8c**
	12.36	3.44	52.59	455.33	Buff	Aq. EtOH	
6.62	11.56	4.16	64.45	$C_{26}H_{20}N_4O_4S$	90	202–204	**9a**
6.55	11.39	4.17	64.39	484.53	Buff	DMF/EtOH	
12.81	11.19	4.03	62.38	$C_{26}H_{20}N_4O_3S_2$	85	207–209	**9b**
12.69	11.22	4.11	62.40	500.59	Buff	DMF/EtOH	
—	10.54	3.79	58.76	$C_{26}H_{20}N_4O_4Se$	85	175–177	**9c**
	10.39	3.63	58.59	531.42	Buff	DMF/EtOH	
6.83	14.92	4.08	63.95	$C_{25}H_{19}N_5O_3S$	75	213–214	**13a**
6.72	14.79	4.01	63.75	469.52	Yellow	DMF/EtOH	
6.24	13.64	3.73	60.81	$C_{26}H_{19}N_5O_5S$	76	236–238	**13b**
6.20	13.59	3.66	60.77	513.52	Yellow	DMSO	
6.27	13.69	4.93	65.74	$C_{28}H_{25}N_5O_3S$	75	187–189	**13c**
6.20	13.66	4.90	65.59	511.59	Yellow	DMF	
6.63	14.48	4.38	64.58	$C_{26}H_{21}N_5O_3S$	65	170–173	**13d**
6.55	14.45	4.33	64.52	483.54	Yellow	DMF/EtOH	
6.77	14.79	4.04	60.88	$C_{24}H_{19}N_5O_4S$	70	220–222	**13e**
6.71	14.66	4.00	60.95	473.5	Yellow	DMF	
6.28	16.46	3.55	61.17	$C_{26}H_{18}N_6O_4S$	72	289–290	**13f**
6.21	16.33	3.49	61.09	510.52	Orange	DMF/EtOH	
6.12	13.38	3.27	61.94	$C_{27}H_{17}N_5O_5S$	78	234–236	**13g**
6.00	13.31	3.11	61.70	523.52	Red	DMF/EtOH	
13.21	14.42	3.94	61.84	$C_{25}H_{19}N_5O_2S_2$	72	245–247	**14a**
13.09	14.31	3.79	61.77	485.58	Orange	DMF/EtOH	

(Continued on next page)

Table I Characterization data of the newly synthesized compounds *(Continued)*

% Analyses, Calcd./Found				Mol. Formula	Yield[a]%	Mp, °C	Compound
S	N	H	C	Mol. Wt.	Color	Solvent	no.
12.11	13.22	3.62	58.97	$C_{26}H_{19}N_5O_4S_2$	70	247–249	**14b**
12.00	13.09	3.69	58.89	529.59	Pale orange	DMF	
12.15	13.27	4.78	63.73	$C_{28}H_{25}N_5O_2S_2$	70	181–184	**14c**
12.01	13.09	4.71	63.66	527.66	Pale orange	DMF	
12.84	14.02	4.24	62.50	$C_{26}H_{21}N_5O_2S_2$	74	267–269	**14d**
12.90	14.21	4.05	62.41	499.61	Orange	DMF	
13.10	14.31	3.91	58.88	$C_{24}H_{19}N_5O_3S_2$	76	251–253	**14e**
13.01	14.19	3.82	58.69	489.57	Yellow	DMF	
12.18	15.96	3.45	59.30	$C_{26}H_{18}N_6O_3S_2$	78	> 300	**14f**
12.09	16.02	3.33	59.49	526.59	Pale orange	DMF/EtOH	
11.89	12.98	3.18	60.10	$C_{27}H_{17}N_5O_4S_2$	80	241–243	**14g**
11.79	12.78	3.01	60.00	539.58	Red	DMF/EtOH	
—	12.74	4.95	67.75	$C_{31}H_{27}N_5O_5$	66	267–269	**20a**
	12.69	4.79	67.69	549.58	Yellow	$CHCl_3$/MeOH	
—	11.49	5.13	65.02	$C_{33}H_{31}N_5O_7$	64	244–246	**20b**
	11.33	5.23	64.92	609.63	Orange	$CHCl_3$/MeOH	
—	11.80	4.58	64.75	$C_{32}H_{27}N_5O_7$	60	252–254	**20c**
	11.77	4.66	64.96	593.59	Orange	$CHCl_3$/MeOH	
5.67	12.38	4.81	65.82	$C_{31}H_{27}N_5O_4S$	61	260–263	**21a**
5.61	12.49	4.78	65.69	565.64	Orange	$CHCl_3$/MeOH	
5.12	11.19	4.99	63.35	$C_{33}H_{31}N_5O_6S$	62	181–182	**21b**
5.00	11.30	4.89	63.46	625.69	Orange	$CHCl_3$/MeOH	
5.26	11.49	4.46	63.04	$C_{32}H_{27}N_5O_6S$	66	267–269	**21c**
5.16	11.36	4.33	63.22	609.65	Orange	$CHCl_3$/MeOH	
6.60	14.42	3.94	61.85	$C_{25}H_{19}N_5O_4S$	78	251–253	**26a**
6.67	14.53	3.81	61.79	485.51	Yellow	EtOH	
7.25	12.66	4.10	65.14	$C_{24}H_{18}N_4O_3S$	68	228–231	**29a**
7.16	12.73	4.00	65.01	442.49	Yellow	Acetic acid	
13.99	12.22	3.96	62.86	$C_{24}H_{18}N_4O_2S_2$	65	221–223	**29b**
13.82	12.00	3.82	62.89	458.56	Yellow	Acetic acid	

Synthesis of Ethyl 3-(4-(Benzoxazol-2-ylphenyl)-2-imino-1,3,4-thiadiazoline-5-carboxylate (4a), Ethyl 3-(4-(Benzothiazol-2-ylphenyl)-2-imino-1,3,4-thiadiazoline-5-carboxylate (4b), and Ethyl 3-(4-(Benzoxazol-2-ylphenyl)-2-imino-1,3,4-selenadiazoline-5-carboxylate (4c)

Method A. A mixture of the appropriate **2a,b** (0.005 mol) and the appropriate amount of potassium thiocyanate (or potassium selenocyanate) (0.006 mol) in ethanol (25 mL) was stirred at room temperature for 24 h. The resulting solid was collected, washed with water, and crystallized from ethanol to give **4a,b** and **4c**, respectively (Tables I and II).

Method B. A mixture of the appropriate **2a,b** (0.005 mol) and thiourea (0.38 g, 0.005 mol) in ethanol (25 mL) was refluxed for 3 h. The solid product that formed after cooling was collected and crystallized from ethanol to give products identical in all respects (mp, mixed mp, and spectra) with **4a** and **4b**, respectively.

Table II ^{1}H NMR spectroscopic data of some synthesized compounds

Spectral data	Compound
IR: 3258 (NH), 3055 (CH, aromatic), 2981 (CH, aliphatic), 1747 (CO), 1605 (C=C), 1476 (CH_2), 1363 (CH_3)	**2a**
^{1}H NMR: $\delta = 1.37$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.40 (d, 2H, $J = 8$Hz, ArH's), 7.50 (d, 2H, $J = 8$Hz, ArH's), 8.00 (d, 2H, $J = 8$Hz, ArH's), 8.07 (d, 2H, $J = 8$Hz, ArH's) and 10.89 (s, br., 1H, NH).	
IR: 3132 (NH), 3055 (CH, aromatic), 2926 (CH, aliphatic), 1743 (CO), 1605 (C=C), 1476 (CH_2), 1355 (CH_3)	**2b**
^{1}H NMR: $\delta = 1.37$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.40 (d, 2H, $J = 8$Hz, ArH's), 7.50 (d, 2H, $J = 8$Hz, ArH's), 8.00 (d, 2H, $J = 8$Hz, ArH's), 8.07 (d, 2H, $J = 8$Hz, ArH's) and 10.89 (s, br., 1H, NH).	
IR: 3462 (NH), 3057 (CH,aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**4a**
^{1}H NMR: $\delta = 1.41$(t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.36–8.36 (m, 9H, ArH's and NH protons)	
IR: 3460 (NH), 30.55 (CH,aromatic), 2981 (CH, aliphatic), 1729 (CO, ester), 1636 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**4b**
^{1}H NMR: $\delta = 1.41$(t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.34 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.36–8.36 (m, 9H, ArH's and NH protons)	
IR: 3463 (NH), 30.55 (CH,aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1636 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**4c**
^{1}H NMR: $\delta = 1.26$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.31 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.38–8.28 (m, 8H, ArH's), 9.85 (s, br., 1H, NH, exchangable)	
IR: 3055 (CH,aromatic), 2984 (CH, aliphatic), 1720 (CO, ester), 1636 (C=N), 1550 (NO), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**5a**
^{1}H NMR: $\delta = 1.41$(t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.36–8.36 (m, 8H, ArH's)	
IR: 3055 (CH,aromatic), 2980 (CH, aliphatic), 1722 (CO, ester), 1636 (C=N), 1603 (C=C), 1535 (NO), 1476 (CH_2), 1663 (CH_3).	**5b**
^{1}H NMR: $\delta = 1.41$(t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.36–8.36 (m, 8H, ArH's)	
IR: 3057 (CH,aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1628 (C=N), 1603 (C=C), 1537 (NO), 1476 (CH_2), 1663 (CH_3).	**5c**
^{1}H NMR: $\delta = 1.35$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.38 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.39–8.36 (m, 8H, ArH's)	
IR: 3055 (CH,aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1685 (CO), 1660 (CO, conjugated), 1636 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**7a**
^{1}H NMR: $\delta = 1.44$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.47 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.27–8.36 (m, 8H, ArH's)	
IR: 3055 (CH,aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1683 (CO), 1636 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**7b**
^{1}H NMR: $\delta = 1.44$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.47 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.27–8.38 (m, 8H, ArH's)	
IR: 3057 (CH,aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1685 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**7c**
^{1}H NMR: $\delta = 1.44$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 4.47 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.27–8.36 (m, 8H, ArH's)	
IR: 3057 (CH,aromatic), 2983 (CH, aliphatic), 1725 (CO, ester), 1685 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**8a**
^{1}H NMR: $\delta = 1.45$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 2.41 (s, 3H, CH_3CO=N), 4.47 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.27–8.44 (m, 8H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1683 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**8b**
^{1}H NMR: $\delta = 1.45$ (t, 3H, $J = 7.5$ Hz, $CH_2\mathbf{CH_3}$), 2.41 (s, 3H, CH_3CO=N), 4.47 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.27–8.44 (m, 8H, ArH's)	

(Continued on next page)

Table II ^{1}H NMR spectroscopic data of some synthesized compounds *(Continued)*

Spectral data	Compound
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1683 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**8c**
^{1}H NMR: δ = 1.45 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.32 (s, 3H, CH_3CO=N), 4.41 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.44–8.42 (m, 8H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1675 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**9a**
^{1}H NMR: δ = 1.46 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.43 (s, 3H, 4-$CH_3C_6H_4$), 4.53 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.26–8.50 (m, 12H, ArH's)	
IR: 3050 (CH,aromatic), 2981 (CH, aliphatic), 1725 (CO, ester), 1678 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**9b**
^{1}H NMR: δ = 1.46 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.43 (s, 3H, 4-$CH_3C_6H_4$), 4.53 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.26–8.50 (m, 12H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1674 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**9c**
^{1}H NMR: δ = 1.34 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.36 (s, 3H, 4-$CH_3C_6H_4$), 4.41 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.32–8.48 (m, 12H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**13a**
^{1}H NMR: δ = 1.36 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 4.39 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.48–8.33 (m, 13H, ArH's), 8.57 (s, 1H, CH=)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1466 (CH_2), 1653 (CH_3).	**13b**
^{1}H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 4.41 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 6.10 (s, 2H, OCH_2O), 7.01–8.30 (m, 11H, ArH's), 8.44 (s, 1H, CH=)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**13c**
^{1}H NMR: δ = 1.28 (d, 6H, $(\mathbf{CH_3})_2CH$, 1.36 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.99 (sex, 1H, $(CH_3)_2\mathbf{C}H$, 4.39 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.23–8.35 (m, 12H, ArH's), 8.46 (s, 1H, CH=)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**13d**
^{1}H NMR: insoluble	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**13e**
^{1}H NMR: δ = 1.37 (t, 3H, J = 7.5 Hz, $\mathbf{CH_3}\mathbf{CH_2}$), 2.35 (s, 3H, CH_3), 4.35 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 6.35 (s, 1H, furan H-4), 7.48–8.38 (m, 10H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1680 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**13f**
^{1}H NMR: δ = 1.36 (t, 3H, $\mathbf{CH_3}CH_2$, 4.42 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 6.85–8.38 (m, 12H, ArH's), 8.46 (s, br., 1H, NH)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1695 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**13g**
^{1}H NMR: δ = 1.35 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 4.38 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.42–8.51 (m, 12H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14a**
^{1}H NMR: δ = 1.36 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 4.39 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.48–8.33 (m, 13H, ArH's), 8.57 (s, 1H, CH=)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14b**
^{1}H NMR: δ = 1.35 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 4.41 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 6.10 (s, 2H, OCH_2O), 6.98–8.23 (m, 11H, ArH's), 8.42 (s, 1H, CH=)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14c**
^{1}H NMR: δ = 1.28 (d, 6H, $(\mathbf{CH_3})_2CH$), 1.36 (t, 3H, J = 7.5 Hz, $CH_2\mathbf{CH_3}$), 2.99 (sex, 1H, $(CH_3)_2\mathbf{C}H$, 4.39 (q, 2H, J = 7.5 Hz, $\mathbf{CH_2}CH_3$), 7.23–8.35 (m, 12H, ArH's), 8.46 (s, 1H, CH=)	

Table II ^{1}H NMR spectroscopic data of some synthesized compounds *(Continued)*

Spectral data	Compound
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14d**
^{1}H NMR: insoluble	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14e**
^{1}H NMR: $\delta = 1.37$ (t, 3H, $J = 7.5$ Hz, (**CH_3CH_2**), 2.35 (s, 3H, CH_3), 4.35 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 6.35 (s, 1H, furan H-4), 7.48–8.38 (m, 10H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1682 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14f**
^{1}H NMR: $\delta = 1.36$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 4.42 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 6.85–8.38 (m, 12H, ArH's), 8.46 (s, br., 1H, NH)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1690 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**14g**
^{1}H NMR: $\delta = 1.30$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 4.29 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 7.48–8.48 (m, 12H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**20a**
^{1}H NMR: $\delta = 1.23$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 1.42 (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 2.88 (s, 3H, CH_3), 4.11 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 4.45 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 13H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**20b**
^{1}H NMR: $\delta = 1.23$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 1.42 (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 2.88 (s, 3H, CH_3), 3.47 (s, 3H, OCH_3), 3.72(s, 3H, OCH_3), 4.11 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 4.45 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**20c**
^{1}H NMR: $\delta = 1.23$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 1.42 (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 2.88 (s, 3H, CH_3), 4.11 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 4.45 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 5.91 (s, 2H, OCH_2O), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**21a**
^{1}H NMR: $\delta = 1.23$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 1.42 (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 2.88 (s, 3H, CH_3), 4.11 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 4.45 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 13H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**21b**
^{1}H NMR: $\delta = 1.23$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 1.42 (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 2.88 (s, 3H, CH_3), 3.47 (s, 3H, OCH_3), 3.72(s, 3H, OCH_3), 4.11 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 4.45 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**21c**
^{1}H NMR: $\delta = 1.23$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 1.42 (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 2.88 (s, 3H, CH_3), 4.11 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 4.45 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 5.91 (s, 2H, OCH_2O), 6.67 (s, 1H, pyrimidine H-4), 6.89–8.43 (m, 11H, ArH's)	
IR: 3382 (NH), 3050 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1682 (CO), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**26**
^{1}H NMR: $\delta = 1.39$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 4.42 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 7.42–8.35 (m, 13H, ArH's), 11.42 (s, br., 1H, NH)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**29a**
^{1}H NMR: $\delta = 1.39$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 4.42 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 7.06–8.38 (m, 13H, ArH's)	
IR: 3055 (CH,aromatic), 2983 (CH, aliphatic), 1728 (CO, ester), 1628 (C=N), 1603 (C=C), 1476 (CH_2), 1663 (CH_3).	**29b**
^{1}H NMR: $\delta = 1.39$ (t, 3H, J = 7.5 Hz, **CH_3**CH_2), 4.44 (q, 2H, J = 7.5 Hz, **CH_2**CH_3), 7.08–8.23 (m, 13H, ArH's)	

Synthesis of Ethyl 2-(Azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (5a), Ethyl 2-(Azanitrosomethylene)-3-(benzothiazol-2-ylphenyl)-1,3,4-thiadiazoline-5-carboxylate (5b), and Ethyl 2-(Azanitrosomethylene)-3-(benzoxazol-2-ylphenyl)-1,3,4-selenadiazoline-5-arboxylate (5c)

A cold saturated solution of sodium nitrite (10 mL) was added dropwise to a solution of the appropriate **4a–c** (1 g) in acetic acid (20 mL) in an ice bath while stirring. The reaction mixture was stirred for 30 min. The resulting solid was collected, washed with water, and crystallized from acetone to give **5a–c**, respectively (Tables I and II).

Synthesis of Ethyl 3-(4-Benzoxazol-2-ylphenyl)-2-oxo-1,3,4-thiadiazoline-5-carboxylate (7a,) 3-(4-Benzothiazol-2-ylphenyl)-2-oxo-1,3,4-thiadiazoline-5-carboxylate (7b), and Ethyl 3-(4-Benzoxazol-2-ylphenyl)-2-oxo-1,3,4-selenadiazoline-5-carboxylate (7c)

A solution of the appropriate **5a–c** (0.5 g) in xylene (20 mL) was refluxed for 15 min. Then the solvent was evaporated under reduced pressure. The residue oil was triturated with petroleum ether (40–60°C), and the solid formed was collected and crystallized from the proper solvent to give 1,3,4-thiadiazolinone **7a,b** and 1,3,4- selenadiazolinone **7c**, respectively (Tables I and II).

Acylation of 4a–c

Acetylation. A mixture of the appropriate **4a–c** (1 g) in acetic acid (10 mL) and acetic anhydride (5 mL) was warmed for 5 min at 70°C. The reaction mixture was poured onto ice water (40 mL). The solid was collected and crystallized to give the *N*-acetyl derivatives **8a–c**, respectively (Tables I and II).

Benzoylation. 4-Methybenzoyl chloride (1 mL) was added to a solution of the appropriate **4a–c** (0.5 g) in pyridine (15 mL), and the mixture was refluxed for 10 min, then poured onto ice water (50 mL) and acidified with hydrochloric acid. The resulting product was collected and washed several times with boiling water. The solid was recrystallized from *N,N*-dimethylformamide to give the *N*-4-methylbenzoyl derivatives **9a–c**, respectively (Tables I and II).

Synthesis of Thiadiazolines 13a–g and 14a–g

Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of the appropriate alkyl carbodithioates **10a–g**(**a,b**) or **101a–g**(**a,b**) (0.005 mol) and compound **2** (1.8 g, 0.005 mol) in ethanol (20 mL). The resulting solid, which formed after 30 min, was collected and recrystallized from the proper solvent and gave the corresponding thiadiazolines **13a–g** and **14a–g**, respectively, in a good yield (Tables I and II).

Synthesis of 1,2,4-Triazolo[4,3-a]pyrimidines 20a–c and 21a–c

Method A. A mixture of the appropriate hydrazonoyl chlorides **2a,b** (0.005 mol) and the appropriate **17a–c** (1.9 g, 0.005 mol) in chloroform (20 mL) containing triethylamine (0.75 mL, 0.005 mol) was refluxed for 10 h. Chloroform was evaporated under reduced

pressure, and the residue solid was recrystallized from chloroform/methanol mixture to give **20a–c** and **21a–c**, respectively (Tables I and II).

Method B. Equimolar amounts of the appropriate hydrazonoyl chlorides **2a,b**, **22a–c**, and sodium ethoxide (0.005 mol each) in ethanol (20 mL) were refluxed for 3 h. The reaction mixture was cooled, and the resulting solid was collected and recrystallized from the proper solvent to give products identical in all respects (mp, mixed mp, and spectra) with corresponding products obtained by method A.

Synthesis of Ethyl 4-(4-(Benzo[d]oxazol-2-yl)phenyl)-5-(benzoylimino)-4,5-dihydro-1,3,4-thiadiazole-2-carboxylate (26)

Method A. Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of methyl benzoylcarbodithioate (**24**) (0.005 mol) and compound **2a** (1.8 g, 0.005 mol) in ethanol (20 mL). The resulting solid, which formed after 30 min, was collected and recrystallized from ethanol to give **26** (Tables I and II).

Method B. Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of 5-phenyl-1,3,4-oxadiazole-2-thiol (**27**) (0.005 mol) and compound **2a** (1.8 g, 0.005 mol) in ethanol (20 mL). The resulting solid, which formed after 30 min, was collected and recrystallized from ethanol to give **26** (Tables I and II).

Synthesis of Ethyl 4-(4-(Benzo[d]oxazol-2-yl)phenyl)-4,5-dihydro-5-(phenylimino)-1,3,4-thiadiazole-2-carboxylate (29a) and Ethyl 4-(4-(Benzo[d]thiazol-2-yl)phenyl)-4,5-dihydro-5-(phenylimino)-1,3,4-thiadiazole-2-carboxylate (29b)

Method A. Triethylamine (0.75 mL, 0.005 mol) was added dropwise with stirring to a mixture of methyl phenylcarbamodithioate (**28**) (0.005 mol) and the appropriate amount of hydrazonoyl chlorides **2a** and **2b** (1.8 g, 0.005 mol) in ethanol (20 mL) for 30 min. The resulting solid was collected and recrystallized from acetic acid to give **29a** and **29b**, respectively (Tables I and II).

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